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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Claims 1-26 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants continue to submit that the standard for written description is that one of skill must demonstrate possession of the claimed invention and f a genus, this can be achieved by description of representative species or providing general structural characteristics in combination with function. Applicants submit that the specification provides such description in that applicants have disclosed any number of polymerases that can be modified using a nucleic acid binding domain as claimed, for example, Taq polymerase.

Applicants continue to submit that the specification not only fully describes polymerases for use in the invention, but also provides description of Sso7d nucleic acid binding domains as recited in the claims, such as the structural feature of the genus of Sso7d proteins for use in the invention, *i.e.,* reference SEQ ID NO:2, and provides structural and functional characteristics of proteins encompassed by the genus. Applicants further submit that the specification further describes references that disclose other Sso7d homologs and describes structural analyses of Sso7d and Sac7d when bound to DNA. Applicants continue to submit that the application also teaches that this DNA binding function can be used as a basis for selecting DNA binding domains that can be used to enhance polymerase processivity.

Applicant's complete argument continues to be acknowledged and has been carefully considered, however, are found nonpersuasive for the reasons previously made of record and repeated herein.

It continues that while applicants have disclosed any number of polymerases that can be modified using a nucleic acid binding domain as claimed, it is pointed out to applicants that while applicants do list a number of polymerases as a number of polymerases are known, applicants only teach that two, Delta Taq and Pfu DNA polymerase, of the many known polymerases are able to have their processivity enhanced as a result of the joining of a double stranded nucleic acid binding domain.

Beyond the few disclosed species, it continues that applicants do not describe any other species of the claimed genus or describe this double stranded nucleic acid binding domain joined to any other polymerase domains. While homologs of the Sso7d protein may be known, it is not shown or clear that these homologs would have the same interaction with all polymerase domains.

Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-26 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those methods of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains, wherein the first domain is a sequence-non-specific-double-stranded nucleic acid-binding domain joined to a second domain which is a Taq or Pfu DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic acid-binding domain is Sso7d comprising the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any method of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is any polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any polymerase domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As above, applicants submit that the specification provides multiple examples of enhancement of processivity of polymerases using Sso7d and its homologs. Applicants submit that in addition to the general guidance regarding polymerases and Sso7d proteins provided by the specification, the examples provide data for four exemplary embodiments using two Sso7 proteins (Sso7d and Sac7d) and three polymerases (Taq,

Delta-Taq, and Pfu). Applicants submit that these data provide further evidence that the claims are enabled.

Applicants have also provided a Declaration under 37 C.F.R. § 1.132 by Peter Vander Horn ("the Vander Horn Declaration") in the parent application and Applicants respectfully request that the Declaration, a copy of which is enclosed, be made of record in the instant application, as the same issues are being raised. Applicants submit that the Vander Horn Declaration provides objective reasons further justifying the claimed genus of methods.

Applicants submit that the Sso7d nucleic acid binding domains set forth in the claims are not derived from a novel gene and a natural variation of about 76% occurs within the family (as noted in the Vander Horn Declaration, which is discussed in greater detail below). Applicants submit that Analyses of the structures of Sso7d and Sac7d bound to DNA have been performed by several investigators and the specification directs a practitioner to exemplary references describing such studies .

Applicants submit that Similar x-ray crystallographic analysis has also been performed for the related protein Sac7d *(e.g.,* Robinson, *et al., Nature* 392:202-205, 1998, which reference is cited by Gao *et al.) and* Gao *et al.* additionally compare the Sso7d-DNA complex to the Sac7d-DNA complex. Thus, the specification therefore properly enables the claimed methods. Applicants submit that they have provided objective reasons justifying the percent identity set forth in the claims. Applicants submit that not only does the subject specification provide a full disclosure of the family

of Sso7 proteins, Applicants have provided the Vander Horn declaration, which provides objective reasons justifying the 75% level of identity recited in the claims. Applicants submit that Dr. Vander Horn explains that by following the differences between the family members, those of skill would immediately recognize where the critical and noncritical regions of the proteins are located and Applicants submit that as Dr. Vander Horn notes in his Declaration, to limit the claims to a percentage above that found within the naturally occurring variants is to ignore that nature has provided this road map for introducing mutations.

Applicants further submit that in addition to the natural variations between family members, any competent protein chemist readily understands that non-naturally occurring but conserved substitutions are possible throughout the primary sequences of the prototype proteins as Dr. Vander Horn explains this conventional wisdom at section 9 of his Declaration.

Applicants submit that furthermore, Dr. Vander Horn explains at section 10 of his Declaration that the structural features of the Archaeal protein interaction with DNA had been previously studied by workers such as Gao *et al.* Dr Vander Horn details how this information permits a practitioner to identify the critical binding domains in the proteins, which allows one of skill to focus mutations away from these critical regions so that amino acid residues may be substituted without compromising activity.

Applicants submit that the Vander Horn Declaration thus further illustrates how one of skill in the art can use the large body of knowledge in the art to identify functional

Sso7d variants having the percent identity set forth in the claims without undue experimentation.

In view of the foregoing, the application provides proper guidance such that one of skill can identify a nucleic acid binding domain as claimed and that use it to modify polymerase processivity with a reasonable expectation of success.

Applicant's complete argument continues to be acknowledged and has been carefully considered, however, is found nonpersuasive for the reasons previously made of record and repeated herein.

As above, with respect to applicants submission that the specification provides multiple examples of enhancement of processivity of polymerases using Sso7d and its homologs, the provided examples, using two Sso7 proteins (Sso7d and Sac7d) and three polymerases (Taq, Delta-Taq, and Pfu) are insufficient to enable the breadth of the claimed genus of methods of amplifying a target nucleic acid comprising the use of any sequence-non-specific double-stranded nucleic-acid-binding domain that comprises an amino acid sequence that has a mere 75% identity to the amino acid sequence of SEQ ID NO:2 and is joined to any polymerase domain with error-correcting activity, where the sequence non-specific double-stranded nucleic-acid-binding domain enhances the processivity of the polymerase domain compared to an identical polymerase domain not having the sequence non-specific double-stranded nucleic acid binding domain.

It is appreciated that with regard to naturally occurring 7kDa proteins in the family of Archael DNA-binding proteins there are many family members reported in the literature and these are evolutionarily related allowing for mutations in these domains to be made while conserving the double stranded DNA binding ability.

It continues to be recognized that the art provides knowledge as to a great number of polymerases and additionally knowledge regarding the DNA binding domain of Sso7d and related homologs, however, it is the lack of teaching and knowledge of the interaction between the various polymerases as encompassed by the claimed methods and the ability of Sso7d homologs to increase the processivity of a polymerase domain that is key to applicants claimed invention. It is the knowledge and guidance related to this relationship and interaction between the two different domains that is absent in the art and applicants specification. For this reasons applicants have not sufficiently enabled the breadth of the claimed genus of methods comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is any polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any polymerase domain

As stated previously and above, with regard to applicants submission that the Sso7d nucleic acid binding domains set forth in the claims are not derived from a novel gene and a natural variation of about 76% occurs within the family (as discussed in the Vander Horn Declaration) this variation within the family of proteins does not offer

sufficient guidance as to those necessary features that result in the claimed increase in processivity of a joined DNA polymerase domain. It is likely that this complex interaction is a result of factors of both the double stranded nucleic acid binding domain as well as the specific polymerase domain itself. Applicants have not addressed this interaction.

In view of the foregoing, the application provides insufficient guidance such that one of skill could not identify those nucleic acid binding domains encompassed in the claims and use it to modify any polymerase domain's processivity with a reasonable expectation of success. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those proteins and methods of their use having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-26 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11, 15, 16 and 22 of copending Application No. 10/306,827. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 11, 15, 16 and 22 of 10/306,827 drawn to a method of increasing the yield of from a polymerase reaction on a target sequence comprising contacting the target nucleic acid with a polymerase joined to a sequence non-specific-nucleic –acid-binding domain anticipate

claims 1-14 drawn to a method of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain. While the preambles of the different claims are different, the method steps of the claims of 10/306,827 anticipate the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's acknowledgement of this provisional rejection and statement that they will consider the filing of a terminal disclaimer to obviate the rejection is acknowledged.